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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,835	05/04/2005	Markus Krumme	RO4037US (#90568)	8149

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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,835	KRUMME, MARKUS	
	Examiner	Art Unit	
	Kevin S. Orwig	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-8 and 10-27* is/are pending in the application.

4a) Of the above claim(s) *10-12,16,17 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-8, 13-15, 18, 19, and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendments and arguments filed Nov. 4, 2009 are acknowledged and have been fully considered. Claims 1-4, 6-8, and 10-27 are now pending. Claims 5 and 9 are cancelled; claims 1-3, 6, 7, and 18 are amended; claims 10-12, 16, 17, and 20-22 are withdrawn; claims 23-27 have been added. Claims 1-4, 6-8, 13-15, 18, 19, and 23-27 are now under consideration.

OBJECTIONS/REJECTIONS WITHDRAWN

The objection to the oath/declaration is withdrawn in light of the English language declaration filed 8/20/09.

The rejections of claims 2, 7, and 18 under 35 U.S.C. 112, 2nd paragraph are withdrawn in light of the claim amendments.

The rejections of claims 5 and 9 are moot in light of the claim cancellations.

The rejection of claims 1-3, 7-9, and 19 under 35 U.S.C. 103(a) over YUKIMATSU is withdrawn in light of the claim amendments.

The rejection of claims 1-3, 7-9, and 19 under 35 U.S.C. 103(a) over RAULT and RUPPRECHT is withdrawn in light of the claim amendments.

OBJECTIONS/REJECTIONS MAINTAINED

The rejection of claims 4-6, 13-15, and 18 under 35 U.S.C. 103(a) is maintained as discussed below.

The double patenting rejections of record have been maintained as no action regarding these rejections has been taken by applicants at this time.

Claim Rejections - 35 USC § 103 (Maintained)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4, 6, 13-15, 18 and now claims 1-3, 7, 8, 19, and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over YUKIMATSU (U.S. 4,740,365; Issued Apr. 26, 1988) and RUPPRECHT (WO 01/03917, Published Jan. 18, 2001) as evidenced by U.S. 2002/0142036 (hereinafter '036).

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Since the WO document to Rupprecht is in German, U.S. 2002/0142036, the U.S. continuation of WO 01/03917 is relied upon herein as an English language equivalent. Paragraph numbers regarding Rupprecht refer to '036.

1. Yukimatsu discloses a two-layer sustained release preparation for application to mucous membranes in the oral cavity (abstract; col. 2, lines 14-16; col. 3, lines 22-54). The preparations have a film-like shape (col. 3, lines 16-21; col. 4, lines 40-42). Yukimatsu teaches that a first layer comprises an active ingredient and one or more polymers including polyvinyl alcohol and a copolymer of maleic anhydride and methyl vinyl ether (i.e. poly(methyl vinyl ether maleic anhydride), elected species) (col. 3, lines 32-37; Example 7). Yukimatsu teaches that a second layer comprises an active ingredient and one or more polymers including polyvinyl alcohol, a copolymer of maleic anhydride and methyl vinyl ether (i.e. poly(methyl vinyl ether maleic anhydride), elected species), and polyacrylic acid polymers and salts thereof (i.e. polyacrylates) (col. 3, lines 42-51). Yukimatsu teaches that the layers function to release the active ingredients in moderate or highly sustained rates (col. 3, lines 55-66). Yukimatsu does not explicitly teach each the use of a neutralized polymethyl methacrylate in the backing layer. However, the use of these components is no more than an obvious variation of Yukimatsu's compositions.

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2. For example, Rupprecht discloses transmucosal multi-layered films made of film-forming polymers (abstract). The films contain and active substance containing layer and a covering (i.e. backing) layer. Rupprecht teaches that preferred cover (i.e. backing) layer materials are films formed from mixtures of polymers and teaches that

Eudragit E (i.e. a neutralized polymethyl methacrylate according to par. [0027] of the instant application) is a suitable preferred cover layer material (par. [0014]). Rupprecht also teaches that mixtures of polymers may be used in the backing layer to optimize the properties of this layer, which Rupprecht teaches include mechanical stabilization of the film, diffusion prevention of the active substance, unidirectional release of the active substance, and adjustment of the sustained release profile of the active agent (pars. [0010], [0015], and [0024]-[0026]). In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to select a neutralized polymethyl methacrylate as a component of the backing layer. One would have been motivated to do so with a high expectation of success since Yukimatsu teaches the use of polyacrylates in the backing layer and since Rupprecht teaches that mixtures of polymers can be used to optimize the release properties of the backing layer and teaches Eudragit E as a preferred component of the backing layer. Thus, the combination of Yukimatsu and Rupprecht renders claims 1-3, 8, and 19 obvious.

3. Regarding the limitations of solubility and swelling, these characteristics are properties inherent to the particular polymers. Yukimatsu addresses the same problem in the art, namely providing sustained release mucoadhesive preparations with sufficient adhesion in the oral cavity. Since the purpose of Yukimatsu's invention is the very same as that instantly claimed and since Yukimatsu (and Rupprecht) discloses the very same polymers for this purpose, it is reasonable that the preparations would have the same characteristics. This interpretation is consistent with Yukimatsu's disclosure since it is clear that the preparations are intended to remain intact in the aqueous environment

of the oral cavity for a long period of time, for example 4 to 24 hours (i.e. they are insoluble or poorly soluble in the oral aqueous media) and that the preparations are swollen by saliva (col. 6, lines 33-41). Thus, in the absence of evidence to the contrary, Yukimatsu's mucoadhesive layer swells in aqueous media, but is insoluble or poorly soluble in the aqueous media. Furthermore, the polyacrylate-containing layer would necessarily reduce the permeation of water and the diffusion of active substance relative to the other layer, as in the instant application. The U.S. Patent Office is not equipped with analytical instruments to test prior art compositions for the infinite number of ways that a subsequent applicant may present previously unmeasured characteristics. When as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is properly shifted to applicant to show otherwise.

4. Yukimatsu teaches that the desired sustained-release properties of the active ingredient and the feel of the preparation can be modulated by adjusting the ratio of the polymer components in the composition (col. 2, line 63 to col. 3, line 8; col. 6, lines 51-68). Thus, by selecting the appropriate combination of polymers, Yukimatsu clearly teaches that any of the disclosed polymers is suitable to achieve the purpose of the invention with no more than routine experimentation. It is noted that the MPEP states that the selection of known materials based on their suitability for their intended uses is *prima facie* obvious. See MPEP § 2144.07. "Reading a list and selecting a known

compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.).

5. Regarding claim 2, the term "mainly consists of" is construed as "consists essentially of". The MPEP states that the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original). "A consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355. Furthermore, the MPEP states that if an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. *In re De Lajarte*, 337 F.2d 870, 143 USPQ 256 (CCPA 1964).

6. In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use poly(methyl vinyl ether maleic anhydride) with polyvinyl alcohol and a polyacrylate, to provide a suitable mucoadhesive layer. One would have been motivated to do so with a high expectation of success

since Yukimatsu teaches a two-layer mucoadhesive composition wherein one layer may comprise polyvinyl alcohol, a copolymer of maleic anhydride and methyl vinyl ether and polyacrylates.

7. Regarding claim 4, Yukimatsu teaches that crosslinked polymers can be used in either of the two layers (col. 2, lines 50-55; col. 4, lines 1-5). Furthermore, one would be motivated to select crosslinked polymers for the mucoadhesive layer in light of Rupprecht.

8. Rupprecht discloses transmucosal multi-layered films made of film-forming polymers (abstract). The films contain and active substance containing layer and a covering (i.e. backing) layer. The active substance layer may be produced from suitable film-forming water-soluble polymers that are crosslinked (pars. [0019] and [0023]). Rupprecht teaches that the ratio of crosslinking agent (i.e. the amount of crosslinking) may be varied to optimize the film properties such as the active substance release properties of the film (pars. [0021] and [0023]). In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to select a cross-linked polymer as taught by Yukimatsu. One would have been motivated to do so with a high expectation of success since Yukimatsu teaches the use of crosslinked polymers in either of the two layers and since Rupprecht teaches that the amount of crosslinking can be adjusted to optimize the release properties of the film. Thus, the combination of Yukimatsu and Rupprecht renders claim 4 obvious.

9. Yukimatsu teaches that polyethylene glycol (i.e. a plasticizer as defined in the instant application) can be present in either layer, rendering claim 6 obvious.

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10. It is noted that there remains an issue of indefiniteness with claim 7 (see 112 2nd par. rejection below). For the purposes of this rejection, the claim has been interpreted to mean that at least one identical polymer is required between the two layers. Yukimatsu teaches that the adjacent layers of the preparation may comprise at least one identical polymer (col. 3, lines 32-54), rendering claim 7 obvious.

11. Yukimatsu teaches that the active agent along with the polymer components is dissolved in a solvent that is dried to form the film-like preparation wherein the active agent is in a solid solution with the polymer (col. 3, lines 18-21; col. 5, lines 36-42; Examples 11 and 15). Furthermore, Rupprecht explicitly teaches that incorporation of the active agent is preferably carried out by dissolving the active substance(s) or, if necessary, emulsifying and/or suspending the active substance(s) in the form of liquid or solid particles in solutions of the crosslinking agent (par. [0051]). In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to incorporate the active substance in a form such as dissolved, suspended, or emulsified. The combination of Yukimatsu and Rupprecht renders claim 13 obvious.

12. Yukimatsu teaches that the active agent may be present in both layers (col. 3, lines 32-54), but does not explicitly teach the use of a concentration gradient. However, Rupprecht teaches that the layers of the film preferably contain the same active substance, each layer having a different respective release profile. Rupprecht teaches that the substance containing layers may exhibit horizontal and/or vertical gradients of the active substance (pars. [0024]-[0025]; claim 1). In light of these teachings, it would

have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to prepare a transmucosal film wherein each layer contained the same active substance as taught by Yukimatsu at different concentrations as taught by Rupprecht. One would have been motivated to do so with a high expectation of success since Yukimatsu teaches a two-layer mucoadhesive composition wherein each layer comprises an active substance and since Rupprecht teaches that formulating the active substances in concentration gradients is preferred. A skilled artisan would have understood the advantages of using a gradient of active agent(s), for example to adjust the sustained release profile of the film. Thus, the combination of Yukimatsu and Rupprecht renders claim 14 obvious.

13. According to the instant specification, diffusion and permeation properties can be modified by varying the pigment content and/or by admixing suitable polymers (e.g. cellulose compounds) (see par. [0041]). Consistent with the instant specification, Yukimatsu teaches the inclusion of a variety of polymers (including cellulose compounds) and conventional additives in both layers (col. 3, lines 32-54; col. 4, lines 16-26), and since Rupprecht teaches the use of both pigments and various polymers (including cellulose compounds) these additives would necessarily modify the solubility and diffusion coefficient of the active substance. Yukimatsu and Rupprecht render claim 15 obvious.

14. Yukimatsu teaches the use of polyacrylic acid (i.e. polyacrylates in an aqueous environment at physiological pH) in layer II, but does not explicitly embody polyacrylates in both layers. However, Rupprecht teaches that both the active substance layer and

the cover layer can preferably be based on anionic polymers such as polyacrylates (pars. [0013], [0014], [0022], [0023], and [0047]; claims 8 and 11). In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include polyacrylates (or polyacrylic acid) in both layers of the dosage form. One would have been motivated to do so with a high expectation of success since Yukimatsu teaches that the desired sustained-release of the active ingredient can be modified by using the combination of various polymers, and since Rupprecht teaches that polyacrylates are preferred base polymers for both layers. Thus, in optimizing the formulation of the layers based on Yukimatsu's teachings, Rupprecht would guide one to include polyacrylates in both layers. Thus, the combination of Yukimatsu and Rupprecht renders claims 18 and 27 obvious.

Rupprecht teaches that the function of the backing layer can be expanded by incorporating colored pigments or other auxiliary substances into the layer to optimize its properties (par. [0016]; claim 10). Yukimatsu also teaches the use of conventional additives in the backing layer (col. 3, lines 53-54). In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to incorporate pigments into the cover layer as taught by Rupprecht. One would have been motivated to do so with a high expectation of success since Yukimatsu teaches the use of conventional additives in this layer and since Rupprecht teaches that colored pigments can be added to optimize the properties of use. A skilled artisan would have understood the advantages of incorporating a colored pigment, for

example to improve consumer appeal. Thus, the combination of Yukimatsu and Rupprecht renders claim 25 obvious.

16. Regarding claim 26, it is noted that the term "matrix former" is not defined in the instant specification. However, the polymers taught by Yukimatsu and Rupprecht are necessarily matrix formers, and thus read on the claim. This interpretation is consistent with the specification, for example, par. [0047], which states that, "The polymers of the individual layers form a polymer matrix which may serve as the active substance reservoir." Claim 26 is rendered obvious by Yukimatsu and Rupprecht.

Response to Arguments

Applicants' arguments have been fully considered but are not persuasive. Applicants argue that there is no motivation to combine the cited references (response, p. 12).

At the outset, it is noted that, in making this argument, applicant is ignoring all of the specific motivations put forward in the previous Office Action. Moreover, applicant is reminded that both Yukimatsu and Rupprecht are directed to highly similar, *if not identical*, problems in the art, namely the construction of film-shaped layered mucoadhesive pharmaceuticals. Moreover, the references teach highly overlapping sets of components for each of the layers and teach that adjustment of the components affects the drug release and other properties of the compositions. Thus, any ordinary artisan would have had significant motivation to combine these references.

Applicant argues that Yukimatsu does not teach neutralized polyacrylate in both layers (response, p. 13).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The deficiency referred to by applicant was acknowledged in the prior Office Action and Rupprecht was relied upon to cure it.

Applicant argues that polyacrylic acid and polyacrylate are different. Applicants mention a reference in support of their argument (Rompp Chemie Lexikon), but no such reference could be located in the file wrapper (response, p. 13).

The term "polyacrylate" has not been defined in the instant specification. It is noted that Webster's Dictionary defines "polyacrylate" as "a polymer of an acrylate : a salt or ester of polyacrylic acid". Thus, while included in the definition of "polyacrylates", polyacrylates are not limited to only esters of polyacrylic acid as applicant incorrectly states. Salts of poly acrylic acid (i.e. the ionized form of polyacrylic acid) are included as well. Both Yukimatsu and Rupprecht teach salts of polyacrylic acid. More importantly, Rupprecht teaches polyacrylates (see pars. [0013], [0014], [0022], [0023], and [0047]; claims 8 and 11). Thus, even if, *in arguendo*, applicant was correct, the point would be moot in light of Rupprecht.

Applicant argues that since the backing layer of Rupprecht does not contain an active substance, the use of Rupprecht's components is not obvious (response, p. 14).

This argument is confusing since Yukimatsu himself teaches that both layers can contain an active agent. Again, applicant is ignoring motivation pointed to in Rupprecht

(e.g. mechanical stabilization of the film, diffusion prevention of the active substance, unidirectional release of the active substance, and adjustment of the sustained release profile of the active agent (pars. [0010], [0015], and [0024]-[0026]). It is unclear how this explicit motivation to use Rupprecht's teachings and components would not motivate the suggested combination. Moreover, Rupprecht teaches that both the active substance containing layer and the backing layer can be based on polyacrylates (pars. [0013], [0014], and [0022]).

Applicant argues that, individually, the references do not teach all of the components instantly claimed for the various layers (response, p. 14).

First, applicant is arguing against the references individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Second, Yukimatsu teaches a layer comprising an active agent, polyvinyl alcohol, a copolymer of maleic anhydride and methyl vinyl ether, and polyacrylic acid or a pharmaceutically acceptable salt thereof (i.e. polyacrylates as discussed above). Third, both references teach adjusting the type and amount of polymers to obtain the desired release profile and properties. Thus, applicant has done nothing more than rearrange elements of the prior art to obtain nothing more than predictable results.

It must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more

than one would expect from such an arrangement, the combination is obvious." *KSR v. Teleflex*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. A.G. Pro*, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (*Id.*). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR v. Teleflex*, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." *Id.* at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of the polymers disclosed by Yukimatsu and Rupprecht, to arrive at compositions "yielding no more than one would expect from such an arrangement." This is particularly true here since both references suggest different combinations to achieve different drug release profiles and properties.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yukimatsu and Rupprecht as evidenced by U.S. 2002/0142036 as applied to claims 1-4, 6-8, 13-15, 18, 19, and 25-27 above, and further in view of TAPOLSKY (WO 98/17251; Published Apr. 30, 1998).

17. The teachings of Yukimatsu and Rupprecht are presented *supra*. Neither reference teaches the use of penetration enhancers *per se*, although it is noted that

compounds such as polyethylene glycol, which are taught by the references, are known penetration enhancers. Nonetheless, Tapolsky is cited to provide applicant a better picture of the prior art and further illustrate how the claimed invention is unpatentable given the state of the art.

18. Tapolsky discloses a film-shaped pharmaceutical delivery device for application of pharmaceutical to mucosal surfaces. The device comprises an adhesive layer and a non adhesive backing layer, and the pharmaceutical may be provided in either or both layers. The device adheres to mucosal surfaces and the kinetics of drug delivery can be adjusted by varying the number of layers and/or the components of the layers (abstract). Tapolsky teaches that a permeation enhancer may be added to the device to improve the absorption of the drug, and provides a list of enhancers that overlaps with that in the instant specification (p. 16, lines 10-17). In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include a penetration enhancer in the compositions of Yukimatsu. One would have been motivated to do so to improve absorption of the drug as taught by Tapolsky. Yukimatsu, Rupprecht, and Tapolsky Render claim 23 obvious.

Claims 6, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yukimatsu and Rupprecht as evidenced by U.S. 2002/0142036 as applied to claims 1-4, 6-8, 13-15, 18, 19, and 25-27 above, and further in view of RAULT (U.S. 6,242,004; Issued Jun. 5, 2001; of record).

19. The teachings of Yukimatsu and Rupprecht are presented *supra*. Neither reference teaches the use solubilizers *per se*, although it is noted that compounds such as polyethylene glycol, which are taught by the references, are known solubilizers.

20. Rault discloses multilayered bioadhesive compounds for transmucosal administration of active substances (abstract; col. 1, lines 3-5 and 49-51). Rault teaches that the compositions are tablets that have a flat or oblong shape (i.e. film-shaped) to ensure the best prolonged maintenance. Rault teaches that various excipients can be included in the layers if need be (i.e. as determined by the skilled artisan). The excipients taught by Rault include absorption promoters (i.e. penetration enhancers), solubilizing agents, and plasticizers (col. 6, lines 6-16). In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include a conventional excipient such as a penetration enhancer, solubilizer, and/or plasticizer in the compositions of Yukimatsu as would be determined by the skilled artisan. Yukimatsu, Rupprecht, and Tapolsky Render claims 6, 23, and 24 obvious.

Double Patenting (Maintained)

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

U.S. Patent Application No. 11/408,958

Claims 1-4, 6-8, 13-15, 18, 19, and 23-27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, and 7-9 of copending Application No. 11/408,958 in view of Rault and Rupprecht. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the '958 claims renders obvious that of the instant claims. The difference between the two claim sets is that the '958 claims recite rapid release from one layer and slow release from another layer. However, this element, and thus the entire scope of the instant claims is rendered obvious since, the instant claim 14 recites at least two layers containing an active substance at different concentrations, which would meet the limitations of the '958 claims. Thus, the instant claims represent an obvious variation of the '958 claims.

Claims 1-9, 13-15, 18, and 19 are directed to an invention not patentably distinct from claims 1-4, and 7-9 of commonly assigned 11/408,958. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/408,958, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35

U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Response to Arguments

Applicants' arguments have been fully considered but are not persuasive. Applicants argue that there are differences in how the drugs are released in the copending applications (response, pgs. 9-10).

Applicant is arguing the intended use of both formulations, which does not carry patentable weight. Any alleged differences in drug release are irrelevant since they are not reflected in the '958 claims. Given the fact that the '958 claims recite exactly the same materials (which are also arranged in the same way), no modification is required, in contrast to applicant's incorrect assertion, and the structure of the preparations in both cases is either identical or an obvious variant in light of the prior art as previously discussed.

NEW GROUNDS OF OBJECTION/REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 13-15, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rault in view of Rupprecht and Tapolsky as evidenced by U.S. 2002/0142036 (hereinafter '036).

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21 Rault discloses multilayered bioadhesive compounds for transmucosal administration of active substances (abstract; col. 1, lines 3-5 and 49-51). Rault teaches that the compositions are tablets that have a flat or oblong shape (i.e. film-shaped) to ensure the best prolonged maintenance of the form on its site of action (col. 7, lines 31-34). The excipients taught by Rault include absorption promoters (i.e. penetration enhancers), solubilizing agents, and plasticizers (col. 6, lines 6-16). Advantageously, the bioadhesive layer Rault's compositions is composed of a maleic

anhydride polymer, preferably a copolymer of methylvinylether and maleic anhydride (i.e. poly(methyl vinyl ether maleic anhydride) (col. 2, lines 38-42). Rault teaches that in an advantageous embodiment, the bioadhesive material (i.e. copolymer of methylvinylether and maleic anhydride) is mixed with at least one swelling agent including polyvinyl alcohol and polymethylmethacrylates (col. 2, lines 63; col. 3, lines 6-7). Rault teaches that the bioadhesive matrix may be crosslinked (col. 2, lines 57-65; col. 3, line 20). Rault teaches that it is advantageous to include a barrier (i.e. backing) layer as a barrier to the diffusion of active principle and to the penetration of water/biological fluid (col. 2, lines 17-21). Rault teaches that the barrier layer(s) are formed from the active principle and a swelling agent (which may be a polyacrylate) (col. 2, lines 60-61). Rault does not teach the active agent in both layers.

22. However, Tapolsky discloses a film-shaped pharmaceutical delivery device for application of pharmaceutical to mucosal surfaces. The device comprises an adhesive layer and a non adhesive backing layer, and the pharmaceutical may be provided in either or both layers. The device adheres to mucosal surfaces and the kinetics of drug delivery can be adjusted by varying the number of layers and/or the components of the layers (abstract). Thus, the placement of the active in both layers obvious to a skilled artisan.

23. Additionally, Rupprecht discloses transmucosal multi-layered films made of film-forming polymers (abstract). The films contain and active substance containing layer and a covering (i.e. backing) layer. Moreover, Rupprecht teaches that preferred cover (i.e. backing) layer materials are films formed from mixtures of polymers and teaches

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that Eudragit E (i.e. a neutralized polymethyl methacrylate according to paragraph [0027] of the instant application) is a suitable preferred cover layer material (paragraph [0014]). Rupprecht also teaches that mixtures of polymers may be used in the backing layer to optimize the properties of this layer, which Rupprecht teaches include mechanical stabilization of the film, diffusion prevention of the active substance, unidirectional release of the active substance, and adjustment of the sustained release profile of the active agent (paragraphs [0010], [0015], and [0024]-[0026]).

24. In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use polyacrylates in the backing layer. One would have been motivated to do so with a high expectation of success since Rault teaches the use of polyacrylates, and since Rupprecht teaches that polyacrylates are preferred base polymers for the backing layer. It is noted that the MPEP states that the selection of known materials based on their suitability for their intended uses is *prima facie* obvious. See MPEP § 2144.07. "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.). Thus, the combination of Rault, Rupprecht, and Tapolsky renders claims 1-4, 6-8, 13-15, 18, 19, and 23-27 obvious.

Response to Arguments

Applicants' arguments have been fully considered but are not persuasive. Applicant argues that Rault is drawn to tablets and asserts that they are "clearly different" from film shaped systems (response, p. 15).

Applicant is reminded that Rault teaches the compositions are tablets that have a flat or oblong shape (i.e. film-shaped) to ensure the best prolonged maintenance of the form on its site of action. Nothing in the instant claims distinguishes from Rault's teachings.

Applicant's argument with respect to Rupprecht is addressed *supra*, and that discussion is incorporated herein.

Regarding the obviousness rejections herein, it is noted that a reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, in the absence of evidence to the contrary, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 18 are indefinite in the recitation "chemically related" in line two of the claim. This phrase is unclear and does not have a generally recognized standard definition in the art. Further, no definition or discussion of this phrase is presented in the specification. Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and the metes and bounds of this claim are indefinite.

Response to Arguments

Applicant states that claims 7 and 18 have been amended. The amendments are noted, but do not resolve the issue of indefiniteness previously raised. The minor wording change is still indefinite for the reasons of record.

Summary/Conclusion

Claims 1-4, 6-8, 13-15, 18, 19, and 23-27 are rejected; claims 5 and 9 are cancelled.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin S. Orwig whose telephone number is (571)270-5869. The examiner can normally be reached Monday-Friday 7:00 am-4:00 pm (with alternate Fridays off). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached Monday-Friday 8:00 am-5:00 pm at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin S Orwig/

/David J Blanchard/
Primary Examiner, Art Unit 1643